

United States Patent 1191

Goodman et al.

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[54]	CANCEROUS B CELL TREATMENT USING	4,643,992	2/1987	Goodman et al
	SUBSTITUTED NUCLEOSIDE DERIVATIVES	4,724,213	2/1988	Epstein
		4,746,651	5/1988	Goodman
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Related U.S. Application Data

Continuation-in-part of Ser. No. 975,830, Nov. 13, 1992, abandoned, which is a continuation-in-part of Ser. No. 945,215, Sep. 15, 1992, Pat. No. 5,317,013, which is a division of Ser. No. 562,101, Aug. 2, 1990, Pat. No. 5,147, 636, which is a division of Ser. No. 361,974, Jun. 9, 1989, Pat. No. 4,948,730, which is a division of Ser. No. 14,618, Feb. 13, 1987, Pat. No. 4,849,411, which is a continuation of Ser. No. 546,679, Nov. 1, 1983, Pat. No. 4,643,992, which is a continuation-in-part of Ser. No. 439,846, Nov. 9, 1982, Pat. No. 4,539,205.

[51]	Int. Cl.6	 A61K 39/39; A61K 31/70;
		C12N 5/06; C12N 5/08

435/240.2

Field of Search 514/26, 34, 45, 514/171, 188, 885, 908; 424/178.1, 181.1, 278.1; 435/240.2

[56] References Cited

U.S. PATENT DOCUMENTS

4,539,205	9/1985	Goodman et al 514/45
4,596,676	6/1986	Cullinan 540/478

4,643,992 2/1987 Goodman et al. 514/4 4,724,213 2/1988 Epstein 424/1. 4,746,651 5/1988 Goodman 514/4 4,801,688 1/1989 Laguzza et al. 530/391 4,814,438 3/1989 Armour et al. 536/27. 4,948,730 8/1990 Goodman et al. 424/1. 5,166,141 11/1992 Goodman et al. 514/4 5,317.013 5/1994 Goodman et al. 514/4

OTHER PUBLICATIONS

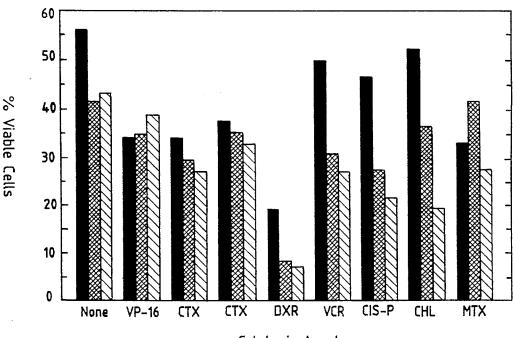
Goodman et al., (1991) Blood 78(suppl. 1)=437(a) Abstr. No. 1738.

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ABSTRACT [57]

Processes for the killing of cancerous B cells, and particularly chronic lymphocytic leukemia (CLL) cells are disclosed. In one process, cancerous B cells that do not proliferate when contacted with an immune response-enhancing agent are contacted with an amount of such an agent sufficient to cause peripheral CLL cells to undergo blast transformation and proliferation. The contacted cells are then maintained for a time period sufficient for them to die from that contact. Further contacting of those cells with a cytotoxic amount of an anti-cancer drug or cytotoxic conjugate enhances the death of those cancer cells. In another process, peripheral CLL cells that proliferate on contact with an immune response-enhancing-agent are contacted with a proliferation-inducing amount of such an agent. The contacted cells are maintained for a time period sufficient to undergo blast transformation and proliferation, and the blasts are then contacted with a cytotoxic amount of an anti-cancer drug or cytotoxic conjugate and maintained.

32 Claims, 7 Drawing Sheets



Cytotoxic Agent